

WHAT IS CLAIMED IS:

1. Isolated nucleic acid having at least 80% nucleic acid sequence identity to:

(a) a nucleotide sequence that encodes the amino acid sequence shown in Figure 2 (SEQ ID NO:2), or Figure 4 (SEQ ID NO:4);

(b) a nucleotide sequence that encodes the amino acid sequence shown in Figure 2 (SEQ ID NO:2), or Figure 4 (SEQ ID NO:4), lacking its associated signal peptide;

(c) a nucleotide sequence that encodes the extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), or Figure 4 (SEQ ID NO:4), with its associated signal peptide;

(d) a nucleotide sequence that encodes the extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), or Figure 4 (SEQ ID NO:4), lacking its associated signal peptide;

(e) the nucleotide sequence shown in Figure 1 (SEQ ID NO:1), or Figure 3 (SEQ ID NO:3);

(f) the full-length coding sequence of the nucleotide sequence shown in Figure 1 (SEQ ID NO:1), or Figure 3 (SEQ ID NO:3); or

(g) the complement of (a), (b), (c), (d), (e), or (f).

2. Isolated nucleic acid comprising:

(a) a nucleotide sequence that encodes the amino acid sequence shown in Figure 2 (SEQ ID NO:2), or Figure 4 (SEQ ID NO:4);

(b) a nucleotide sequence that encodes the amino acid sequence shown in Figure 2 (SEQ ID NO:2), or Figure 4 (SEQ ID NO:4), lacking its associated signal peptide;

(c) a nucleotide sequence that encodes the extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), or Figure 4 (SEQ ID NO:4), with its associated signal peptide;

(d) a nucleotide sequence that encodes the extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), or Figure 4 (SEQ ID NO:4), lacking its associated signal peptide;

(e) the nucleotide sequence shown in Figure 1 (SEQ ID NO:1), or Figure 3 (SEQ ID NO:3);

(f) the full-length coding sequence of the nucleotide sequence shown in Figure 1 (SEQ ID NO:1), or Figure 3 (SEQ ID NO:3); or

(g) the complement of (a), (b), (c), (d), (e), or (f).

3. Isolated nucleic acid that hybridizes to:

(a) a nucleotide sequence that encodes the amino acid sequence shown in Figure 2 (SEQ ID NO:2), or Figure 4 (SEQ ID NO:4);

(b) a nucleotide sequence that encodes the amino acid sequence shown in Figure 2 (SEQ ID NO:2), or Figure 4 (SEQ ID NO:4), lacking its associated signal peptide;

(c) a nucleotide sequence that encodes the extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), or Figure 4 (SEQ ID NO:4), with its associated signal peptide;

(d) a nucleotide sequence that encodes the extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), or Figure 4 (SEQ ID NO:4), lacking its associated signal peptide;

(e) the nucleotide sequence shown in Figure 1 (SEQ ID NO:1), or Figure 3 (SEQ ID NO:3);

(f) the full-length coding sequence of the nucleotide sequence shown in Figure 1 (SEQ ID NO:1), or Figure



3 (SEQ ID NO:3); or

(g) the complement of (a), (b), (c), (d), (e), or (f).

4. The nucleic acid of Claim 3, wherein the hybridization occurs under stringent conditions.

5 5. The nucleic acid of Claim 3 which is at least about 5 nucleotides in length.

6. An expression vector comprising the nucleic acid of Claim 1.

7. The expression vector of Claim 6, wherein said nucleic acid is operably linked to control sequences  
10 recognized by a host cell transformed with the vector.

8. A host cell comprising the expression vector of Claim 7.

9. The host cell of Claim 8 which is a CHO cell, an *E. coli* cell or a yeast cell.

15

10. A process for producing a polypeptide comprising culturing the host cell of Claim 8 under conditions suitable for expression of said polypeptide and recovering said polypeptide from the cell culture.

11. An isolated polypeptide having at least 80% amino acid sequence identity to:

20

(a) the amino acid sequence shown in Figure 2 (SEQ ID NO:2), or Figure 4 (SEQ ID NO:4);

(b) the amino acid sequence shown in Figure 2 (SEQ ID NO:2), or Figure 4 (SEQ ID NO:4), lacking its associated signal peptide;

(c) an amino acid sequence of the extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), or Figure 4 (SEQ ID NO:4), with its associated signal peptide;

25

(d) an amino acid sequence of the extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), or Figure 4 (SEQ ID NO:4), lacking its associated signal peptide;

(e) an amino acid sequence encoded by the nucleotide sequence shown in Figure 1 (SEQ ID NO:1), or Figure 3 (SEQ ID NO:3); or

30 (f) an amino acid sequence encoded by the full-length coding sequence of the nucleotide sequence shown in Figure 1 (SEQ ID NO:1), or Figure 3 (SEQ ID NO:3).

12. An isolated polypeptide comprising:

(a) the amino acid sequence shown in Figure 2 (SEQ ID NO:2), or Figure 4 (SEQ ID NO:4);

35 (b) the amino acid sequence shown in Figure 2 (SEQ ID NO:2), or Figure 4 (SEQ ID NO:4), lacking its associated signal peptide;

(c) an amino acid sequence of the extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), or Figure 4 (SEQ ID NO:4), with its associated signal peptide;

(d) an amino acid sequence of the extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), or Figure 4 (SEQ ID NO:4), lacking its associated signal peptide;



(e) an amino acid sequence encoded by the nucleotide sequence shown in Figure 1 (SEQ ID NO:1), or Figure 3 (SEQ ID NO:3); or

(f) an amino acid sequence encoded by the full-length coding sequence of the nucleotide sequence shown in Figure 1 (SEQ ID NO:1), or Figure 3 (SEQ ID NO:3).

5           13.     A chimeric polypeptide comprising the polypeptide of Claim 11 fused to a heterologous polypeptide.

14.     The chimeric polypeptide of Claim 13, wherein said heterologous polypeptide is an epitope tag sequence or an Fc region of an immunoglobulin.

10           15.     An isolated antibody which binds to a polypeptide having at least 80% amino acid sequence identity to:

(a) the amino acid sequence shown in Figure 2 (SEQ ID NO:2), or Figure 4 (SEQ ID NO:4);

15           (b) the amino acid sequence shown in Figure 2 (SEQ ID NO:2), or Figure 4 (SEQ ID NO:4), lacking its associated signal peptide;

(c) an amino acid sequence of the extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), or Figure 4 (SEQ ID NO:4), with its associated signal peptide;

(d) an amino acid sequence of the extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), or Figure 4 (SEQ ID NO:4), lacking its associated signal peptide;

20           (e) an amino acid sequence encoded by the nucleotide sequence shown in Figure 1 (SEQ ID NO:1), or Figure 3 (SEQ ID NO:3); or

(f) an amino acid sequence encoded by the full-length coding sequence of the nucleotide sequence shown in Figure 1 (SEQ ID NO:1), or Figure 3 (SEQ ID NO:3).

25           16.     The antibody of Claim 15 which binds to a polypeptide comprising:

(a) the amino acid sequence shown in Figure 2 (SEQ ID NO:2), or Figure 4 (SEQ ID NO:4);

(b) the amino acid sequence shown in Figure 2 (SEQ ID NO:2), or Figure 4 (SEQ ID NO:4), lacking its associated signal peptide;

30           (c) an amino acid sequence of the extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), or Figure 4 (SEQ ID NO:4), with its associated signal peptide;

(d) an amino acid sequence of the extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), or Figure 4 (SEQ ID NO:4), lacking its associated signal peptide;

(e) an amino acid sequence encoded by the nucleotide sequence shown in Figure 1 (SEQ ID NO:1), or Figure 3 (SEQ ID NO:3); or

35           (f) an amino acid sequence encoded by the full-length coding sequence of the nucleotide sequence shown in Figure 1 (SEQ ID NO:1), or Figure 3 (SEQ ID NO:3).

17.     The antibody of Claim 15 which is a monoclonal antibody.



18. The antibody of Claim 15 which is an antibody fragment.

19. The antibody of Claim 15 which is a chimeric or a humanized antibody.

20. The antibody of Claim 15 which is conjugated to a growth inhibitory agent.

21. The antibody of Claim 15 which is conjugated to a cytotoxic agent.

22. The antibody of Claim 21, wherein the cytotoxic agent is selected from the group consisting of toxins, antibiotics, radioactive isotopes and nucleolytic enzymes.

23. The antibody of Claim 21, wherein the cytotoxic agent is a toxin.

24. The antibody of Claim 23, wherein the toxin is selected from the group consisting of maytansinoid and calicheamicin.

25. The antibody of Claim 23, wherein the toxin is a maytansinoid.

26. The antibody of Claim 15 which is produced in bacteria.

27. The antibody of Claim 15 which is produced in CHO cells.

28. The antibody of Claim 15 which induces death of a cell to which it binds.

29. The antibody of Claim 15 which is detectably labeled.

30. The antibody of Claim 15 comprising a variant Fc region with altered neonatal Fc receptor (FcRn) binding affinity, which polypeptide comprises an amino acid modification at any one or more of amino acid positions 238, 252, 253, 254, 255, 256, 265, 272, 286, 288, 303, 305, 307, 309, 311, 312, 317, 340, 356, 360, 362, 376, 378, 380, 382, 386, 388, 400, 413, 415, 424, 433, 434, 435, 436, 439 or 447 of the Fc region, wherein the numbering of the residues in the Fc region is that of the EU index as in Kabat.

31. The antibody of claim 30 which displays increased binding to FcRn.

32. The antibody of claim 31 which displays increased binding to FcRn and comprises an amino acid modification at any one or more of amino acid positions 238, 256, 265, 272, 286, 303, 305, 307, 311, 312, 317, 340, 356, 360, 362, 376, 378, 380, 382, 413, 424 or 434 of the Fc region, wherein the numbering of the residues in the Fc region is that of the EU index as in Kabat.

33. The antibody of claim 32 wherein said amino acid modification is at any one or more of amino



acid positions 305, 307, 311, 312, 317, 360, 362, 380, 382, 424 or 434 of the Fc region, wherein the numbering of the residues in the Fc region is that of the EU index as in Kabat.

34. An isolated nucleic acid comprising a nucleotide sequence that encodes the antibody of Claim 15.

5 35. An expression vector comprising the nucleic acid of Claim 34 operably linked to control sequences recognized by a host cell transformed with the vector.

36. A host cell comprising the expression vector of Claim 35.

10 37. The host cell of Claim 36 which is a CHO cell, an *E. coli* cell or a yeast cell.

38. A process for producing an antibody comprising culturing the host cell of Claim 36 under conditions suitable for expression of said antibody and recovering said antibody from the cell culture.

15 39. A composition of matter comprising:  
(a) the polypeptide of Claim 11;  
(b) the chimeric polypeptide of Claim 13; or  
(c) the antibody of Claim 15, in combination with a carrier.

20 40. The composition of matter of Claim 39, wherein said carrier is a pharmaceutically acceptable carrier.

41. An article of manufacture:  
(a) a container; and  
25 (b) the composition of matter of Claim 39 contained within said container.

42. The article of manufacture of Claim 41 further comprising a label affixed to said container, or a package insert included with said container, referring to the use of said composition of matter for the therapeutic treatment of or the diagnostic detection of a cancer.

30 43. A method of killing a cancer cell that expresses a polypeptide having at least 80% amino acid sequence identity to:

(a) the amino acid sequence shown in Figure 2 (SEQ ID NO:2), or Figure 4 (SEQ ID NO:4); or  
(b) an amino acid sequence encoded by a nucleotide sequence comprising the nucleotide sequence shown  
35 in Figure 1 (SEQ ID NO:1), or Figure 3 (SEQ ID NO:3),  
said method comprising contacting said cancer cell with an antibody that binds to said polypeptide on said cancer cell, thereby killing said cancer cell.

44. The method of Claim 43, wherein said antibody is a monoclonal antibody.



45. The method of Claim 43, wherein said antibody is an antibody fragment.
46. The method of Claim 43, wherein said antibody is a chimeric or a humanized antibody.
47. The method of Claim 43, wherein said antibody is conjugated to a growth inhibitory agent.
- 5 48. The method of Claim 43, wherein said antibody is conjugated to a cytotoxic agent.
49. The method of Claim 48, wherein said cytotoxic agent is selected from the group consisting of  
toxins, antibiotics, radioactive isotopes and nucleolytic enzymes.
- 10 50. The method of Claim 48, wherein the cytotoxic agent is a toxin.
51. The method of Claim 50, wherein the toxin is selected from the group consisting of maytansinoid  
and calicheamicin.
- 15 52. The method of Claim 50, wherein the toxin is a maytansinoid.
53. The method of Claim 43, wherein said antibody is produced in bacteria.
- 20 54. The method of Claim 43, wherein said antibody is produced in CHO cells.
55. The method of Claim 43, wherein said cancer cell is further exposed to radiation treatment or a  
chemotherapeutic agent.
- 25 56. The method of Claim 43, wherein said antibody comprises a variant Fc region with altered  
neonatal Fc receptor (FcRn) binding affinity, which polypeptide comprises an amino acid modification at any one  
or more of amino acid positions 238, 252, 253, 254, 255, 256, 265, 272, 286, 288, 303, 305, 307, 309, 311, 312,  
317, 340, 356, 360, 362, 376, 378, 380, 382, 386, 388, 400, 413, 415, 424, 433, 434, 435, 436, 439 or 447 of the  
Fc region, wherein the numbering of the residues in the Fc region is that of the EU index as in Kabat.
- 30 57. The method of Claim 56, wherein said antibody displays increased binding to FcRn.
58. The method of Claim 56, wherein said antibody displays increased binding to FcRn and  
comprises an amino acid modification at any one or more of amino acid positions 238, 256, 265, 272, 286, 303,  
305, 307, 311, 312, 317, 340, 356, 360, 362, 376, 378, 380, 382, 413, 424 or 434 of the Fc region, wherein the  
35 numbering of the residues in the Fc region is that of the EU index as in Kabat.
59. The method of Claim 58, wherein said amino acid modification is at any one or more of amino  
acid positions 305, 307, 311, 312, 317, 360, 362, 380, 382, 424 or 434 of the Fc region, wherein the numbering



of the residues in the Fc region is that of the EU index as in Kabat.

60. The method of Claim 43, wherein said cancer cell is selected from the group consisting of a breast cancer cell, a colorectal cancer cell, a lung cancer cell, an ovarian cancer cell, a central nervous system cancer cell, a liver cancer cell, a bladder cancer cell, a pancreatic cancer cell, a cervical cancer cell, a melanoma cell, a leukemia cell and a glioma cell.

61. The method of Claim 60, wherein said cancer cell is a glioma cell.

62. The method of Claim 43, wherein said cancer cell overexpresses said polypeptide as compared to a normal cell of the same tissue origin.

63. A method of therapeutically treating a mammal having a tumor comprising cells that express a polypeptide having at least 80% amino acid sequence identity to:

(a) the amino acid sequence shown in Figure 2 (SEQ ID NO:2), or Figure 4 (SEQ ID NO:4); or

(b) an amino acid sequence encoded by a nucleotide sequence comprising the nucleotide sequence shown in Figure 1 (SEQ ID NO:1), or Figure 3 (SEQ ID NO:3),

said method comprising administering to said mammal a therapeutically effective amount of an antibody that binds to said polypeptide, thereby effectively treating said mammal.

64. The method of Claim 63, wherein said antibody is a monoclonal antibody.

65. The method of Claim 63, wherein said antibody is an antibody fragment.

66. The method of Claim 63, wherein said antibody is a chimeric or a humanized antibody.

67. The method of Claim 63, wherein said antibody is conjugated to a growth inhibitory agent.

68. The method of Claim 63, wherein said antibody is conjugated to a cytotoxic agent.

69. The method of Claim 68, wherein said cytotoxic agent is selected from the group consisting of toxins, antibiotics, radioactive isotopes and nucleolytic enzymes.

70. The method of Claim 68, wherein the cytotoxic agent is a toxin.

71. The method of Claim 70, wherein the toxin is selected from the group consisting of maytansinoid and calicheamicin.

72. The method of Claim 70, wherein the toxin is a maytansinoid.



73. The method of Claim 63, wherein said antibody is produced in bacteria.

74. The method of Claim 63, wherein said antibody is produced in CHO cells.

75. The method of Claim 63, wherein said tumor is further exposed to radiation treatment or a  
5 chemotherapeutic agent.

76. The method of Claim 63, wherein said antibody comprises a variant Fc region with altered neonatal Fc receptor (FcRn) binding affinity, which polypeptide comprises an amino acid modification at any one or more of amino acid positions 238, 252, 253, 254, 255, 256, 265, 272, 286, 288, 303, 305, 307, 309, 311, 312,  
10 317, 340, 356, 360, 362, 376, 378, 380, 382, 386, 388, 400, 413, 415, 424, 433, 434, 435, 436, 439 or 447 of the Fc region, wherein the numbering of the residues in the Fc region is that of the EU index as in Kabat.

77. The method of Claim 76, wherein said antibody displays increased binding to FcRn.

78. The method of Claim 76, wherein said antibody displays increased binding to FcRn and  
15 comprises an amino acid modification at any one or more of amino acid positions 238, 256, 265, 272, 286, 303, 305, 307, 311, 312, 317, 340, 356, 360, 362, 376, 378, 380, 382, 413, 424 or 434 of the Fc region, wherein the numbering of the residues in the Fc region is that of the EU index as in Kabat.

79. The method of Claim 78, wherein said amino acid modification is at any one or more of amino  
20 acid positions 305, 307, 311, 312, 317, 360, 362, 380, 382, 424 or 434 of the Fc region, wherein the numbering of the residues in the Fc region is that of the EU index as in Kabat.

80. The method of Claim 63, wherein said tumor is a breast tumor, a colorectal tumor, a lung tumor,  
25 an ovarian tumor, a central nervous system tumor, a liver tumor, a bladder tumor, a pancreatic tumor, a cervical tumor or a glioma.

81. The method of Claim 80, wherein said tumor is a glioma.

82. A method of determining the presence of a polypeptide in a sample suspected of containing said  
30 polypeptide, wherein said polypeptide has at least 80% amino acid sequence identity to:

(a) the amino acid sequence shown in Figure 2 (SEQ ID NO:2), or Figure 4 (SEQ ID NO:4); or

(b) an amino acid sequence encoded by a nucleotide sequence comprising the nucleotide sequence shown  
in Figure 1 (SEQ ID NO:1), or Figure 3 (SEQ ID NO:3),

35 said method comprising exposing said sample to an antibody that binds to said polypeptide and determining binding of said antibody to said polypeptide in said sample.

83. The method of Claim 82, wherein said sample comprises a cell suspected of expressing said polypeptide.



84. The method of Claim 83, wherein said cell is a cancer cell.

85. The method of Claim 82, wherein said antibody is detectably labeled.

86. The method of Claim 82, wherein said antibody comprises a variant Fc region with altered neonatal Fc receptor (FcRn) binding affinity, which polypeptide comprises an amino acid modification at any one or more of amino acid positions 238, 252, 253, 254, 255, 256, 265, 272, 286, 288, 303, 305, 307, 309, 311, 312, 317, 340, 356, 360, 362, 376, 378, 380, 382, 386, 388, 400, 413, 415, 424, 433, 434, 435, 436, 439 or 447 of the Fc region, wherein the numbering of the residues in the Fc region is that of the EU index as in Kabat.

87. The method of Claim 86, wherein said antibody displays increased binding to FcRn.

88. The method of Claim 86, wherein said antibody displays increased binding to FcRn and comprises an amino acid modification at any one or more of amino acid positions 238, 256, 265, 272, 286, 303, 305, 307, 311, 312, 317, 340, 356, 360, 362, 376, 378, 380, 382, 413, 424 or 434 of the Fc region, wherein the numbering of the residues in the Fc region is that of the EU index as in Kabat.

89. The method of Claim 88, wherein said amino acid modification is at any one or more of amino acid positions 305, 307, 311, 312, 317, 360, 362, 380, 382, 424 or 434 of the Fc region, wherein the numbering of the residues in the Fc region is that of the EU index as in Kabat.

90. A method of diagnosing the presence of a tumor in a mammal, said method comprising detecting the level of expression of a gene encoding a polypeptide having at least 80% amino acid sequence identity to:

(a) the amino acid sequence shown in Figure 2 (SEQ ID NO:2), or Figure 4 (SEQ ID NO:4); or  
(b) an amino acid sequence encoded by a nucleotide sequence comprising the nucleotide sequence shown in Figure 1 (SEQ ID NO:1), or Figure 3 (SEQ ID NO:3),

in a test sample of tissue cells obtained from said mammal and in a control sample of known normal cells of the same tissue origin, wherein a higher level of expression of said polypeptide in the test sample, as compared to the control sample, is indicative of the presence of tumor in the mammal from which the test sample was obtained.

91. The method of Claim 90, wherein the step detecting the level of expression of a gene encoding said polypeptide comprises employing an oligonucleotide in an *in situ* hybridization or RT-PCR analysis.

92. The method of Claim 90, wherein the step detecting the level of expression of a gene encoding said polypeptide comprises employing an antibody in an immunohistochemistry analysis.

93. A method of diagnosing the presence of a tumor in a mammal, said method comprising contacting a test sample of tissue cells obtained from said mammal with an antibody that binds to a polypeptide having at least 80% amino acid sequence identity to:

(a) the amino acid sequence shown in Figure 2 (SEQ ID NO:2), or Figure 4 (SEQ ID NO:4); or



(b) an amino acid sequence encoded by a nucleotide sequence comprising the nucleotide sequence shown in Figure 1 (SEQ ID NO:1), or Figure 3 (SEQ ID NO:3),

and detecting the formation of a complex between said antibody and said polypeptide in the test sample, wherein the formation of a complex is indicative of the presence of a tumor in said mammal.

5           94.       The method of Claim 93, wherein said antibody is detectably labeled.

          95.       The method of Claim 93, wherein said antibody comprises a variant Fc region with altered neonatal Fc receptor (FcRn) binding affinity, which polypeptide comprises an amino acid modification at any one or more of amino acid positions 238, 252, 253, 254, 255, 256, 265, 272, 286, 288, 303, 305, 307, 309, 311, 312,  
10       317, 340, 356, 360, 362, 376, 378, 380, 382, 386, 388, 400, 413, 415, 424, 433, 434, 435, 436, 439 or 447 of the Fc region, wherein the numbering of the residues in the Fc region is that of the EU index as in Kabat.

          96.       The method of Claim 95, wherein said antibody displays increased binding to FcRn.

15           97.       The method of Claim 96, wherein said antibody displays increased binding to FcRn and comprises an amino acid modification at any one or more of amino acid positions 238, 256, 265, 272, 286, 303, 305, 307, 311, 312, 317, 340, 356, 360, 362, 376, 378, 380, 382, 413, 424 or 434 of the Fc region, wherein the numbering of the residues in the Fc region is that of the EU index as in Kabat.

20           98.       The method of Claim 97, wherein said amino acid modification is at any one or more of amino acid positions 305, 307, 311, 312, 317, 360, 362, 380, 382, 424 or 434 of the Fc region, wherein the numbering of the residues in the Fc region is that of the EU index as in Kabat.

          99.       The method of Claim 93, wherein said test sample of tissue cells is obtained from an individual  
25       suspected of having a cancerous tumor.

          100.       An antibody as in claims 30, 56, 76, 86 or 95, further comprising the characteristic of increased binding to FcRn at acidic pH as compared to binding to FcRn at neutral pH.